Method of preparation

Codeine Phosphate	10 g
Lactose	a sufficient quantity
To make	1000 g

Prepare as directed under Powders, with the above ingredients.

Identification Determine the absorption spectrum of a solution of 1% Codeine Phosphate Powder (1 in 100) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 283 nm and 287 nm.

Assay Weigh accurately about 5 g of 1% Codeine Phosphate Powder, dissolve in water to make exactly 100 mL, then pipet 10 mL of this solution, add exactly 10 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of codeine phosphate for assay, separately determined the water in the same manner as Codeine Phosphate, dissolve in water to make exactly 100 mL, then pipet 10 mL of this solution, add exactly 10 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions, and calculate the ratios, Q_T and Q_S, of the peak area of codeine to that of the internal standard.

Amount (mg) of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$)
= amount (mg) of codeine phosphate for assay, calculated on the anhydrous basis
$\times 1.0227 \times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of etilefrine hydrochloride (3 in 10,000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (about 5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.0 g of sodium lauryl sulfate in 500 mL of diluted phosphoric acid (1 in 1000), and adjust the pH to 3.0 with sodium hydroxide TS. To 240 mL of this solution add 70 mL of tetrahydrofuran, and mix.

Flow rate: Adjust the flow rate so that the retention time of codeine is about 10 minutes.

Selection of column: Proceed with 20 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of codeine and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Tight containers.

10% Codeine Phosphate Powder

リン酸コデイン散 10%

10% Codeine Phosphate Powder contains not less than 9.3% and not more than 10.7% of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$: 406.37).

Method of preparation

Codeine Phosphate	100 g
Lactose	a sufficient quantity
To make	1000 g

Prepare as directed under Powders, with the above ingredients.

Identification Determine the absorption spectrum of a solution of 10% Codeine Phosphate Powder (1 in 1000) as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 283 nm and 287 nm.

Assay Weigh accurately about 2.5 g of 10% Codeine Phosphate Powder, dissolve in water to make exactly 100 mL, then pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution and water to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.05 g of codeine phosphate for assay, separately determined the water in the same manner as Codeine Phosphate, dissolve in water to make exactly 100 mL, then pipet 10 mL of this solution, add exactly 10 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following operating conditions, and calculate the ratios, Q_T and Q_S, of the peak area of codeine to that of the internal standard:

Amount (mg) of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$)
= amount (mg) of codeine phosphate for assay, calculated on the anhydrous basis
$\times 1.0227 \times \frac{Q_T}{Q_S} \times 5$

Internal standard solution—A solution of etilefrine hydrochloride (3 in 10,000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.0 g of sodium lauryl sulfate in 500 mL of diluted phosphoric acid (1 in 1000), and adjust the pH to 3.0 with sodium hydroxide TS. To 240 mL of this solution add 70 mL of tetrahydrofuran, and mix.

Flow rate: Adjust the flow rate so that the retention time of codeine is about 10 minutes.

Selection of column: Proceed with 20 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of codeine

and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Tight containers.

Codeine Phosphate Tablets

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Codeine Phosphate Tablets contains not less than 93% and not more than 107% of the labeled amount of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$: 406.37).

Method of preparation Prepare as directed under Tablets, with Codeine Phosphate.

Identification To a quantity of powdered Codeine Phosphate Tablets, equivalent to 0.1 g of Codeine Phosphate according to the labeled amount, add 20 mL of water, shake, and filter. To 2 mL of the filtrate add water to make 100 mL, and determine the absorption spectrum as directed under the Ultraviolet-visible Spectrophotometry: it exhibits a maximum between 283 nm and 287 nm.

Assay Weigh accurately and powder not less than 20 Codeine Phosphate Tablets. Weigh accurately a portion of the powder, equivalent to about 0.1 g of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$), add 30 mL of water, shake, add 20 mL of diluted dilute sulfuric acid (1 in 20), treat the mixture with ultrasonic waves for 10 minutes, and add water to make exactly 100 mL. Filter this solution, then pipet 5 mL of the filtrate, add exactly 10 mL of the internal standard solution and water to make 20 mL, and use this solution as the standard solution. Separately, weigh accurately about 0.05 g of codeine phosphate for assay, separately determined its water content in the same manner as Codeine Phosphate, dissolve in water to make exactly 100 mL, then pipet 10 mL of this solution, add exactly 10 mL of the internal standard solution, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of codeine to that of the internal standard.

Amount (mg) of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4.\frac{1}{2}H_2O$)
= amount (mg) of codeine phosphate for assay, calculated on the anhydrous basis

$$\times 1.0227 \times \frac{Q_T}{Q_S} \times 2$$

Internal standard solution—A solution of etilefrine hydrochloride (3 in 10,000).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 280 nm).

Column: A stainless steel column about 4 mm in inside diameter and 15 to 25 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (about 5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 1.0 g of sodium lauryl sulfate in 500 mL of diluted phosphoric acid (1 in 1000), and adjust the pH to 3.0 with sodium hydroxide TS. To 240 mL of this solution add 70 mL of tetrahydrofuran, and mix.

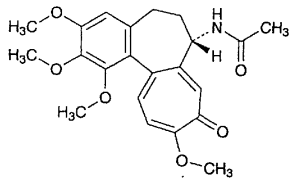
Flow rate: Adjust the flow rate so that the retention time of codeine is about 10 minutes.

Selection of column: Proceed with 20 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of codeine and the internal standard in this order with the resolution between these peaks being not less than 4.

Containers and storage Containers—Tight containers.

Colchicine

コルヒチン



$C_{22}H_{25}NO_6$: 399.44

N-[(7*S*)-(5,6,7,9)-Tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[*a*]heptalen-7-yl)]acetamide [*64-86-8*]

Colchicine, when dried, contains not less than 96.0% of $C_{22}H_{25}NO_6$.

Description Colchicine occurs as a yellowish white powder. It is odorless.

It is freely soluble in acetic anhydride and in ethanol (95), sparingly soluble in water, and very slightly soluble in diethyl ether.

It is colored by light.

Identification **(1)** To 1 mL of a solution of Colchicine in ethanol (95) (1 in 20) add 1 drop of iron (III) chloride TS: a dark reddish orange color is produced.

(2) Mix 1 mg of Colchicine with 2 drops of sulfuric acid in a porcelain dish: a yellow color is produced. On the addition of 1 drop of nitric acid: the color of the solution changes from blue-green through purple to yellow. Add 5 mL of sodium hydroxide TS: the color of the solution changes to reddish.

(3) Dissolve 0.01 g of Colchicine in 0.5 mL of dilute hydrochloric acid and 10 mL of water, and boil under a reflux condenser for 1 hour. Add 40 mL of warm water, shake, and filter while warm. Cool, and extract the filtrate with 20 mL of chloroform. Filter the chloroform extract, and evaporate on a water bath to dryness. Dissolve the residue in 0.5 mL of 1,4-dioxane, and add 10 mL of diethyl ether. Collect the crystals on a filter, wash with small portions of diethyl ether, and dry at 105°C for 1 hour: the crystals so obtained melt between 176°C and 179°C.

Optical rotation $[\alpha]_D^{20}$: −230 – −245° (after drying, 0.1 g, ethanol (95), 10 mL, 100 mm).